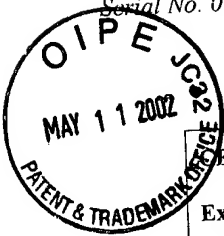


5-14-02

GP1637

Serial No. 09/942,342

Case 4584



CERTIFICATION OF MAILING

CERTIFICATION UNDER 37 CFR 1.10

Express Mail Number: EL 897626083 USDate of Deposit: MAY 10, 2002

I hereby certify that this correspondence is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

TECH CENTER 1600/2900

MAY 16 2002

RECEIVED

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor: Ewing

Attorney Docket No. 4584

Serial No: 09/942,342

Art Unit: 1637

Filed: August 27, 2001

Examiner: J. Riley

Title: NON-FLUORESCENT QUENCHER COMPOUNDS AND
BIOMOLECULAR ASSAY

RESPONSE TO RESTRICTION REQUIREMENT UNDER 37 CFR § 1.111

Assistant Commissioner for Patents
Washington, D. C. 20231

Sir:

With reference to the Office communication mailed April 30, 2002, reconsideration of the application is respectfully requested. Claims 1-75 are pending. In the Office communication mailed April 30, 2002, the claims were divided into nine groups. The restriction is respectfully traversed. Applicant provisionally elects claim group I, claims 1-25, solely to comply with 37 CFR 1.143.

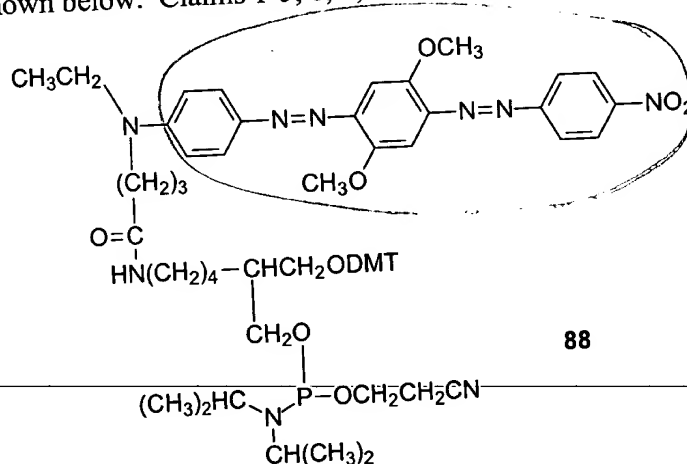
It is noted that Groups II, III, and VI are all composition claims. The Examiner has classified them in the same class 536 and the same subclass 26.6. The Examiner has not provided sufficient substantive basis justifying the restriction of these composition claims. In particular, the Examiner has provided no explanation as to how these claim sets are both independent and distinct.

It is further noted that Groups IV, V, VII, VIII, and IX are all method claims. The Examiner has classified them in the same class 435. Groups V, VIII, and IX are classified in the same

subclass 6. The Examiner has not provided sufficient substantive basis justifying the restriction of these method claims. In particular, the Examiner has provided no explanation as to how these claim sets are both independent and distinct.

Accordingly, the restriction requirement appears to be improper. The applicant maintains that restriction into nine inventions is unduly burdensome and unjustified under 35 USC 121. Reconsideration is respectfully requested.

In response to the requirement for an election of species under 35 USC § 121, applicant provisionally elects the species of compound 88, found at page 57, Example 44 of the specification, and shown below. Claims 1-5, 8, 9, and 18-20 read on the elected species.



*It is not
disclosed
in claims?
not response*

Applicants expressly reserve the right to prosecute claims drawn to the unelected claims and unclaimed subject matter in one or more timely filed continuation, divisional and/or continuation-in-part applications.

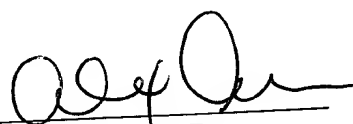
PETITION FOR TIME EXTENSION and FEE AUTHORIZATION

This reply is considered timely filed. If any time extensions are required, such time extensions are hereby requested. If any additional fees not submitted with this response are required, please take such fees from deposit account number 01-2213.

Respectfully submitted,

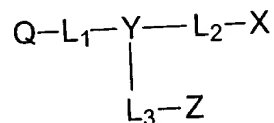
CORRESPONDENCE ADDRESS

Applied Biosystems
850 Lincoln Centre Drive
Foster City, California 94404
TEL: 650 638-5607
FAX: 650 638-6677


Alex Andrus, Ph.D.
Agent for Applicant(s)
Reg. No. 44,509

Appendix:

1. A fluorescence quencher composition having the structure:



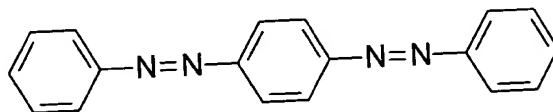
wherein Y is selected from N and CR, where R is H, C₁-C₆ alkyl or C₅-C₁₄ aryl;

L₁, L₂, and L₃ are independently selected from a bond, C₁-C₁₂ alkylidyl, C₁-C₁₂ alkoxyldiyl, C₁-C₁₂ alkylaminodiyl, C₁-C₁₂ alkylamidediyl, C₅-C₁₄ arylidyl, and 1-20 ethyleneoxy units;

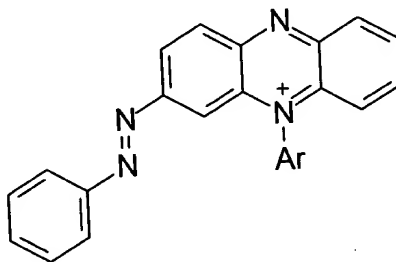
X is an amino acid, a polypeptide, a nucleoside, a nucleotide, a polynucleotide, or a protected form thereof; or X is an acid-labile protecting group;

Z is selected from H, CO₂H, OH, NH₂, NHR, NR₂, SH, an ester, a cleavable linker, a solid support, a reactive linking group, and a label selected from a fluorescent dye, a hybridization-stabilizing moiety, a chemiluminescent dye, and an affinity ligand; and

Q is selected from the diazo structures:

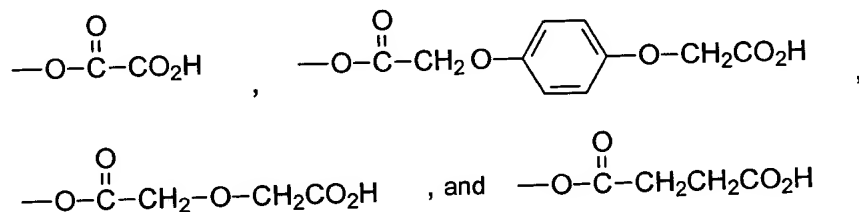


and

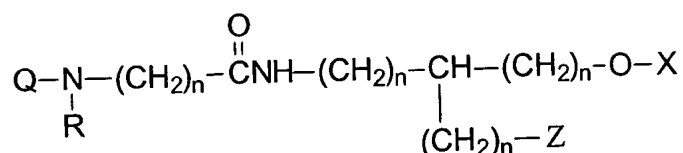
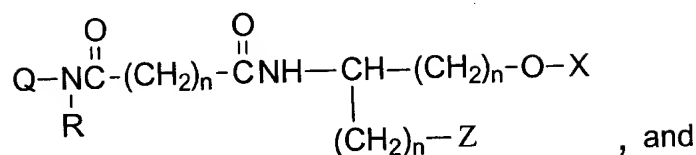
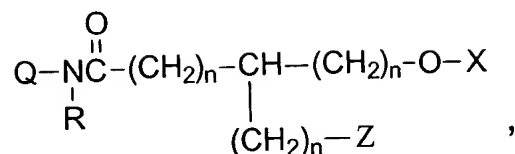


wherein Ar is C₅-C₁₄ aryl; one of the aryl carbons of the diazo structures is the site of attachment to L₁; at least one aryl carbon of each diazo structure is substituted with an electron-withdrawing group and at least one aryl carbon of each diazo structure is substituted with an electron-donating group.

2. The fluorescence quencher composition of claim 1 wherein the electron-withdrawing groups are selected from NO₂, CN, CF₃, CO₂H, CO₂R, C(O)NH₂, C(O)NHR, C(O)NR₂, CHO, C(O)R, SO₂R, SO₂CF₃, SO₂OR, SO₃H, NO, and C₅-C₁₄ aryl, where R is H, C₁-C₁₂ alkyl or C₅-C₁₄ aryl.
3. The fluorescence quencher composition of claim 2 wherein a NO₂ is *para* to a diazo group.
4. The fluorescence quencher composition of claim 1 wherein the electron-donating groups are selected from O⁻, S⁻, NR₂, NHR, NH₂, NHC(O)R, OR, OH, OC(O)R, SR, SH, Br, I, Cl, F, R, and C₅-C₁₄ aryl, where R is H, C₁-C₁₂ alkyl or C₅-C₁₄ aryl.
5. The fluorescence quencher composition of claim 4 wherein a OCH₃ is *ortho* or *meta* to a diazo group.
6. The fluorescence quencher composition of claim 1 where Z is OH
7. The fluorescence quencher composition of claim 1 where Z is an ester selected from the structures:



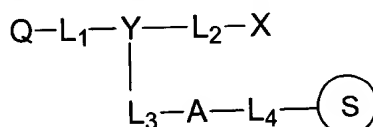
8. The fluorescence quencher composition of claim 1 selected from the structures:



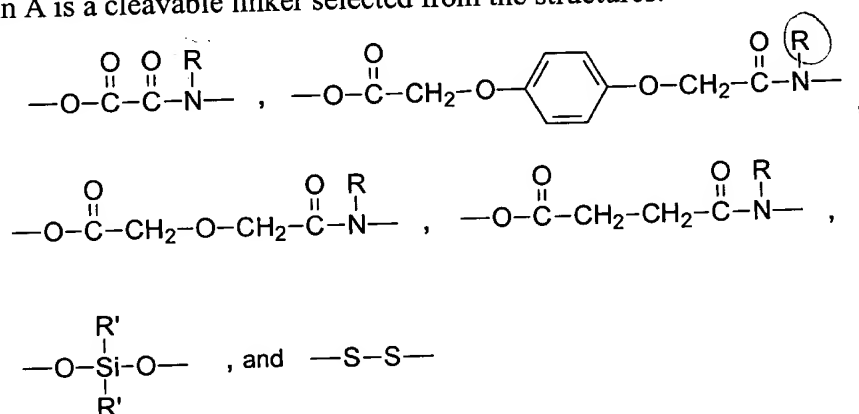
where n is 1 to 12.

9. The fluorescence quencher composition of claim 1 wherein X is selected from DMT, MMT, trityl, substituted trityl, pixyl, and trialkylsilyl.

10. The fluorescence quencher composition of claim 1 having the structure:



wherein A is a cleavable linker selected from the structures:

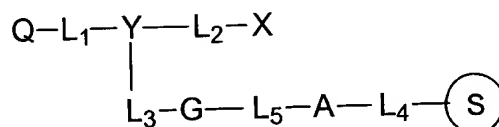


where R' is H, C₁–C₁₂ alkyl or C₁–C₁₂ alkoxy;

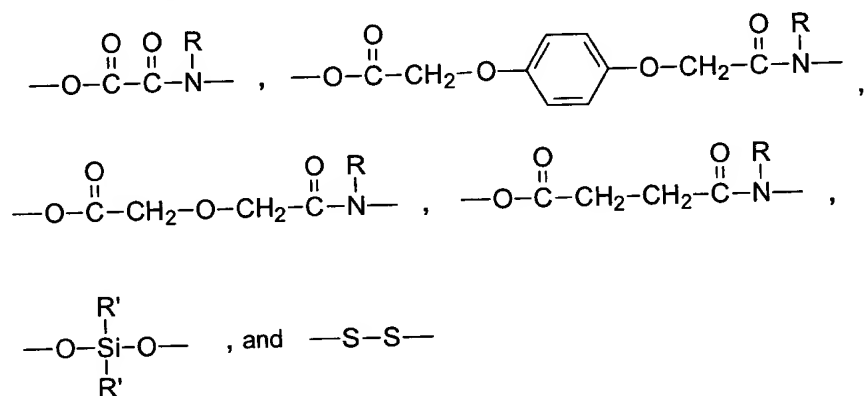
L₄ is selected from a bond, C₁–C₁₂ alkylidyl, C₁–C₁₂ alkoxyldyl, C₁–C₁₂ alkylaminodiy, C₁–C₁₂ alkylamidediyl, C₅–C₁₄ arylidyl, and 1-20 ethyleneoxy units; and

(S) is a solid support.

11. The fluorescence quencher composition of claim 10 wherein X is a nucleotide.
12. The fluorescence quencher composition of claim 10 wherein the solid support is selected from polystyrene, controlled-pore-glass, silica gel, silica, polyacrylamide, polyacrylate, hydroxyethylmethacrylate, polyamide, polyethylene, polyethyleneoxy, and copolymers and grafts of such.
13. The fluorescence quencher composition of claim 10 wherein the form of the solid support is selected from a particle, a bead, a membrane, a frit, a fiber, a tube, a capillary, a slide, a plate, a micromachined chip, an alkanethiol-gold layer, a magnetic bead, a non-porous surface, an addressable array, and polynucleotide-immobilizing medium.
14. The fluorescence quencher composition of claim 1 having the structure:



wherein A is a cleavable linker selected from the structures:



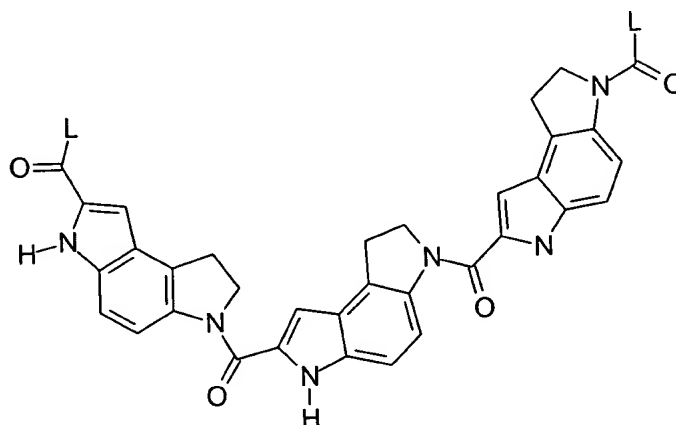
where R is H, C₁-C₁₂ alkyl or C₁-C₁₂ alkoxy;

L₄ and L₅ are independently selected from a bond, C₁-C₁₂ alkylidyl, C₁-C₁₂ alkoxyldyl, C₁-C₁₂ alkylaminodiy, C₁-C₁₂ alkylamidediyl, C₅-C₁₄ aryldiy, and 1-20 ethyleneoxy units;

G is a hybridization-stabilizing moiety; and

(S) is a solid support.

15. The fluorescence quencher composition of claim 14 in which G comprises:

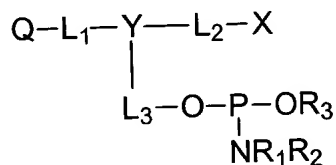


where L are the sites of attachment to L_3 and L_5 .

16. The fluorescence quencher composition of claim 14 wherein the solid support is selected from polystyrene, controlled-pore-glass, silica gel, silica, polyacrylamide, magnetic beads, polyacrylate, hydroxyethylmethacrylate, polyamide, polyethylene, polyethyleneoxy, and copolymers and grafts of such.

17. The fluorescence quencher composition of claim 14 wherein the form of the solid support is selected from a particle, a bead, a membrane, a frit, a fiber, a tube, a capillary, a slide, a plate, a micromachined chip, an alkanethiol-gold layer, a magnetic bead, a non-porous surface, an addressable array, and polynucleotide-immobilizing medium.

18. The fluorescence quencher composition of claim 1 having the structure:

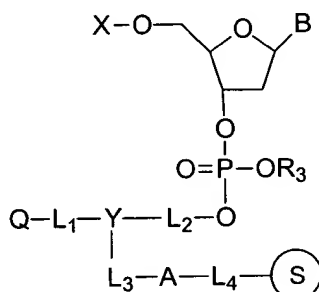


wherein X is an acid-labile protecting group; R_1 and R_2 are individually selected from isopropyl, morpholino, methyl, ethyl and C_5 - C_{14} aryl; R_1 and R_2 taken together are C_4 - C_{11} cycloalkyl or morpholino; and R_3 is C_1 - C_6 alkyl or C_5 - C_{14} aryl.

19. The fluorescence quencher composition of claim 18 wherein R_1 and R_2 are each isopropyl and R_3 is cyanoethyl.

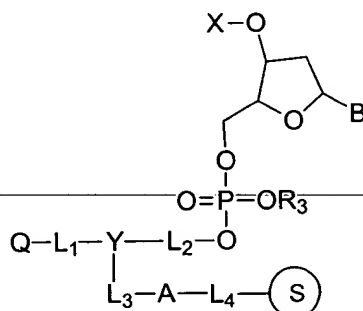
20. The fluorescence quencher composition of claim 18 wherein X is selected from DMT, MMT, trityl, substituted trityl, pixyl, and trialkylsilyl.

21. The fluorescence quencher composition of claim 11 having the structure:



wherein X is an acid-labile protecting group; B is a nucleobase; and R₃ is selected from H, C₁-C₆ alkyl, and C₅-C₁₄ aryl.

22. The fluorescence quencher composition of claim 11 having the structure:



wherein X is an acid-labile protecting group; B is a nucleobase; and R₃ is selected from H, C₁-C₆ alkyl, and C₅-C₁₄ aryl.

23. The fluorescence quencher composition of claim 1 where X is a polynucleotide.

24. The fluorescence quencher composition of claim 23 wherein the polynucleotide comprises one or more N-[2-(aminoethyl)]glycine units having a nucleobase attached to nitrogen through a methylene carbonyl linkage.

25. The fluorescence quencher composition of claim 23 wherein the polynucleotide comprises one or more 2'-4' or 3'-4' bicyclic sugar modifications.